

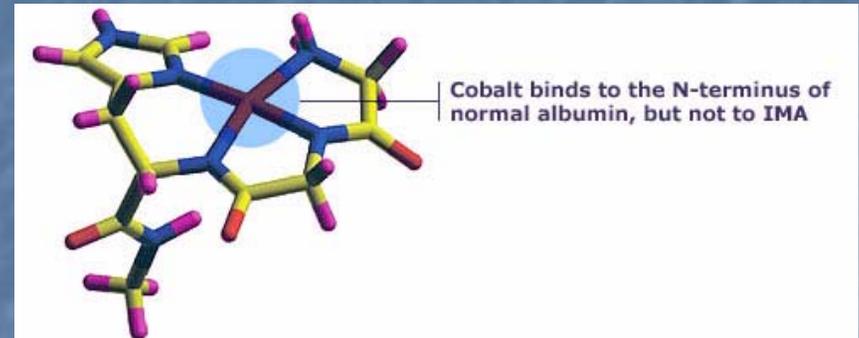
Ischemia-Modified Albumin

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Biochemistry

- During ischemia, N-terminus of albumin is altered, probably through a series of chemical reactions involving free radical damage-altered albumin, termed Ischemia Modified Albumin (IMA)
- IMA is unable to bind metals such as cobalt at the N-terminus
- When albumin circulating in blood comes in contact with ischemic tissue in the heart, some of it is converted to IMA
 - Ischemic patients have proportionately more IMA than non-ischemic patients
 - Produced continually during ischemia, which means its blood concentrations rise quickly and remain elevated during an ischemic event



COBALT ?????

Albumin Cobalt Binding (ACB®) Test

- Cobalt is added to a serum sample
- Cobalt binds to normal albumin, but not to IMA
- ACB test measures unbound cobalt
- Higher levels of unbound cobalt indicate greater concentrations of IMA



Background

- **1990** IMA marker discovered by practicing emergency physician.
- **1992** Pilot clinical study shows IMA elevated in patients with acute myocardial infarction and unstable angina
- **1994** First patent issued on core technology of IMA
- **1997** Ischemia Technologies formed to commercialize IMA marker. Seed capital funding
- **1998** Pilot clinical study shows IMA elevated during angioplasty-induced ischemia
- **1999** ACB® Test developed to measure IMA on clinical chemistry instruments. Series A funding
- **2000** First multicenter clinical trial shows IMA improves diagnostic sensitivity of Troponin I. Series B funding
- **2001** ACB Test CE marked and first sales in Europe. Voluntary certification to ISO9001, ISO13485, and EN46001 achieved. Series C funding.

Instrumentation

- Currently available on the COBAS MIRA Plus and Hitachi 911 analyzers
- Ischemia Technologies to have a point-of-care IMA on the market in 2004

Clinical Trials

- Rises rapidly in response to transient ischemia induced by balloon angioplasty
- Negative IMA (result within normal range) can be used to predict subsequent negative troponin
 - IMA has value as a rule out AMI
 - Twice the sensitivity of cardiac troponin for detecting patients with AMI
 - When used in conjunction with troponin, almost three times as many patients with AMI can be detected from a presentation blood test than with troponin alone
- Early clinical results suggest that IMA will prove useful as a biochemical marker of ischemia
- Multicenter clinical studies are underway to investigate IMA as an aid to diagnosis of cardiac ischemia

Utility

- Positive within six to 10 minutes of an ischemic cardiac event
- IMA returns to baseline about six hours after cessation of an ischemic event, as induced by balloon inflation

Comparison

- Detects the majority of patients with unstable angina and is negative in less than 20 percent of ACS patients
- Troponin has about 14 percent sensitivity in predicting adverse cardiac outcome in the emergency department observation-unit population
- Electrocardiograms miss about half of patients with ACS on initial presentation

Efficacy

- Combination of a negative IMA and troponin and a nondiagnostic ECG yields a negative predictive value of 99 percent
 - Likelihood that the patient has ACS is one percent

Lowered Costs

- Hospitals will pay about \$30 per test for IMA
- 2.5 million people a year who present to the ED with chest pain receive testing that turns up negative
 - If IMA allows hospitals to shift the percentage of patients with chest pain who are sent home from the ED by 10 to 15 percent then the test is extremely valuable, especially when used in a managed care population
 - Hospitals now release about 20 percent of such patients from the ED

False Positives

- Some cancers
- Acute infections
- End-stage renal disease
- Liver cirrhosis
- Brain ischemia

Potential Downside

- Ordering cardiac angiograms based solely on positive IMA results
- Ischemia Technologies is conducting ongoing clinical studies to help define what a positive IMA might mean in terms of guiding therapy and predicting long-term clinical outcomes

Current Recommendations

- Part of cardiac series including:
 - Troponin
 - Myoglobin
 - B-type natriuretic peptide
- Centers for Medicare and Medicaid Services in April 2002 implemented an outpatient carve-out code, APC 0339, that pays for an observation period separately above and beyond the outpatient fee
 - Shift in reimbursement will encourage hospital EDs to use best practices, such as IMA, to perform better risk stratification of patients up front before determining who requires inpatient care

Summary

- Positive within six to 10 minutes of an ischemic cardiac event
- IMA returns to baseline about six hours after cessation of an ischemic event, as induced by balloon inflation
- Combination of a negative IMA and troponin and a nondiagnostic ECG yields a negative predictive value of 99 percent

Questions

- A child of five would understand this. Send someone to fetch a child of five.



"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."

--Groucho Marx

References

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